



Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Metabolic safety of the etonogestrel contraceptive implant in healthy women over a 3-year period



Jaqueline Villas-Boas^{a,b}, Luiz C. Vilodre^{b,c}, Helena Malerba^{b,d}, Mila Pontremoli Salcedo^{e,f}, Mirela Foresti Jiménez^{e,f}, Patrícia El Beitune^{e,f,*}

^a Specialized in Obstetrics and Gynecology, Hysteroscopy, Sexually Transmitted Diseases and Sexual Violence, Porto Alegre, Brazil

^b Department of Obstetrics and Gynecology, Hospital Materno Infantil Presidente Vargas, Porto Alegre, Brazil

^c Obstetrics and Gynecology, Universidade Luterana do Brasil (ULBRA), Porto Alegre, Brazil

^d Public Health Nurse, Porto Alegre, Brazil

^e Department of Obstetrics and Gynecology, Post-Graduate Program, Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA), Porto Alegre, Brazil

^f Services of Obstetrics and Gynecology, Complexo Hospitalar Santa Casa de Porto Alegre (ISCMPA), Porto Alegre, Brazil

ARTICLE INFO

Article history:

Received 29 January 2016

Received in revised form 17 April 2016

Accepted 23 April 2016

Keywords:

Adverse effects

Etonogestrel implant

Long-lasting contraception

Lipid metabolism

Carbohydrate metabolism

Body mass index

ABSTRACT

Objective: To ascertain whether placement of the etonogestrel contraceptive implant induces significant changes in carbohydrate and lipid metabolism, as reflected by metabolic parameters, in healthy women.

Study design: Prospective cohort study of 213 healthy patients who received etonogestrel implants. Weight, BMI, blood pressure and a comprehensive metabolic profile were assessed at baseline, 1, 2 and 3 years. In 21 of the 213 participants, AUC for glucose levels, fasting insulin levels at baseline and year 3 (immediately before implant removal), HOMA-IR score, and the QUICK index were assessed. Parameters were expressed as median and interquartile range. The Wilcoxon test and ANOVA were used for comparison of measurements after implant placement (significance level $p < 0.05$).

Results: Median age was 26 years (range, 22–31.5). Results showed a trend toward increase of the variables weight (63.3–66.1) and BMI (24.7–25.7) and a decrease in TC (172–161.5), TG (75–69.5), and LDL (100.5–98.5) ($p > 0.05$). Of the metabolic variables, FBG (85–88) and HDL (53–46) had significant differences ($p < 0.002$). In the subgroup of 21 patients, there were reductions in insulin levels (9.65 vs. 8.4 mU/dL, $p = 0.03$), HOMA scores (2.06 vs. 1.75, $p = 0.02$), QUICK index (0.34 vs. 0.35, $p = 0.03$), TC (178 vs. 160 mg/dL, $p = 0.001$), HDL (51 vs. 46 mg/dL, $p = 0.009$), and LDL (110 vs. 100 mg/dL, $p = 0.035$).

Conclusion: These results provide evidence of the metabolic safety of the ENG implant in healthy women over a 3-year period. Indeed, implant placement induces changes consistent with a lower risk of insulin resistance and dyslipidemia.

© 2016 Elsevier Ireland Ltd. All rights reserved.

Introduction

The long-lasting etonogestrel (ENG) contraceptive implant contains 68 mg of ENG, is placed subdermally in the non-dominant arm and exerts a contraceptive effect for 3 years [1,2]. The effective contraception provided by long-lasting subdermal implants constitutes a major advance in women's independence. However, it has been speculated that these implants may lead to adverse metabolic effects, including changes in weight, body mass index (BMI), and carbohydrate and lipid metabolism [3].

Few studies have conducted prospective assessments of the safety of this implant in clinically healthy women. The present study evaluated the effects of the etonogestrel (ENG) implant on weight, BMI, total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides (TG), fasting blood glucose (FBG), insulin, area under the blood glucose curve (AUC), homeostatic model assessment of insulin resistance (HOMA-IR) score, quantitative insulin sensitivity check (QUICK) index, and fasting glucose-to-insulin ratio (FGIR), over a 3-year period, with pairwise comparisons at baseline and year 3 (immediately prior to implant removal), in recipients of this mode of contraception.

Research design and methods

A prospective cohort study was conducted between 2007 and 2011 in a sample of 213 ENG implant recipients with a mean age of

* Corresponding author at: Rua Prof. Annes Dias 135, Chefia da Maternidade Mario Totta, CEP: 90020-090, Porto Alegre, RS, Brazil. Tel.: +55 51 32148525.
E-mail address: pbeitune@yahoo.com.br (P. El Beitune).

26 years (range, 22–31.5). Weight, BMI, blood pressure, FBG, TC, HDL, LDL, and TG levels were measured at baseline (pre-implant), 1 year, 2 years, and 3 years. Of these 213 women, 21 agreed to take part in paired data collection, including area under the blood glucose curve (0, 30, 60, 90 and 120 min) and insulin measurements, at baseline and year 3 (immediately prior to implant removal).

All women included in the sample were healthy from a clinical and laboratory standpoint and had been referred to our service by their physicians for specialist contraceptive care. All participants included had no personal or (first-degree) family history of diabetes or endocrine conditions. Unfortunately, we could not obtain reliable data on family history of dyslipidemia, as most participants were unaware of this information.

The study was approved by the relevant institutional research ethics committee and all subjects provided written informed consent for participation. Subjects who had any health conditions, suspected pregnancy, abnormal uterine bleeding of unknown etiology, hypersensitivity to ENG implant components, or required any medication that might affect the evaluated parameters were excluded from the sample, as were those who refused to take part in the study.

Descriptive statistics were expressed as median and interquartile range. The Kolmogorov–Smirnov test was used to assess the distribution of data and the variables were found to be asymmetrically distributed. The Wilcoxon test and ANOVA with Bonferroni's post-hoc procedure were used for statistical analysis. Data were log-transformed for ANOVA. The significance level was set at $p < 0.05$.

Results

Table 1 shows the results of all 213 women included in the study. The median age was 26 years (IQR 22–32), and the most prevalent ethnicities were white (74.6%), black (18.8%), and brown (6.6%). Overall, 23.3% of women were smokers; of these, 6.7% smoked >20 cigarettes/day. Subjects were assessed at four points in time: before implant placement (baseline, T0) and at 1 (T1), 2 (T2), and 3 (T3) years. Blood pressure rates remained constant throughout. On average, weight increased 3 kg and BMI increased 1 kg/m² over the 3-year study period. Blood glucose levels also increased, but remained within normal range. There was a significant reduction in HDL and a trend toward decrease in LDL and TG levels. These findings (blood glucose and HDL) were independent of ethnicity ($p = 0.104$ and $p = 0.602$ respectively) and smoking status ($p = 0.234$ and $p = 0.624$ respectively).

Also described below (Table 2) are the results of pairwise comparison of 21 patients at T0 and T3, only including those

Table 2

Pairwise comparison of anthropometric parameters and lipid and carbohydrate metabolism profile at baseline and year 3 after etonogestrel implant placement in 21 healthy women. Data expressed as median and interquartile range.

| Variable | T0 (n=21) | T3 (n=21) | P ^a |
|--------------------------|------------------------|------------------------|----------------|
| Weight (kg) | 65 (58.5–75.7) | 64.9 (58.1–76.5) | 0.69 |
| BMI (kg/m ²) | 25.9 (22.9–30.2) | 25.6 (22.8–31.8) | 0.70 |
| TC (mg/dL) | 178 (151.5–211.7) | 160 (146.5–174.0) | 0.001 |
| LDL (mg/dL) | 110 (90.0–136.2) | 100 (84.5–113.5) | 0.035 |
| HDL (mg/dL) | 51 (43.0–60.7) | 46 (39.5–53.5) | 0.009 |
| TG (mg/dL) | 79 (57.7–115.2) | 73 (63–95) | 0.70 |
| FBG (mg/dL) | 89 (82.0–93.0) | 88 (82.5–94.0) | 0.259 |
| FI (mU/dL) | 9.65 (5.1–24.0) | 8.4 (5.3–14.7) | 0.03 |
| AUC | 12,720 (11,000–15,020) | 14,180 (11,300–16,760) | 0.21 |
| HOMA | 2.06 (1.19–5.59) | 1.75 (0.98–4.45) | 0.02 |
| QUICK | 0.34 (0.29–0.37) | 0.35 (0.30–0.38) | 0.03 |
| FGIR | 0.11 (0.05–0.26) | 0.09 (0.05–0.18) | 0.13 |

^a Wilcoxon test. AUC, area under the curve; BMI, body mass index; FBG, fasting blood glucose; FGIR, fasting glucose-to-insulin ratio; FI, fasting insulin; HDL, high-density lipoprotein; HOMA, homeostatic model assessment; LDL, low-density lipoprotein; QUICK, quantitative insulin sensitivity check index; TC, total cholesterol; TG, triglycerides.

patients in whom area under the blood glucose curve and insulin concentrations were measured. The median age in this subgroup was 27 years (IQR 22–39), and most women were white (77.3%), black (18.2%), or brown (4.5%). Smokers accounted for 19% of the subgroup. Of these, 4.8% smoked >20 cigarettes/day. Anthropometric parameters and lipid and metabolic profiles are described as medians and interquartile ranges. Significant reductions occurred in insulin levels (9.65 vs. 8.4; $p = 0.03$), HOMA scores (2.06 vs. 1.75; $p = 0.02$), QUICK index (0.34 vs. 0.35; $p = 0.03$), TC (178 vs. 160; $p = 0.001$), HDL (51 vs. 46; $p = 0.009$), and LDL (110 vs. 100; $p = 0.035$) levels between T0 and T3, immediately prior to implant removal. These findings were also independent of smoking status and ethnicity ($p > 0.05$).

Discussion

In the present study, subjects exhibited an average weight gain of 3 kg over the 3-year study period. This finding is similar to that of other authors who reported a mean 2.6% increase in body weight over a 2-year period in the ENG implant group of the study. Despite this tendency to increase, the findings reported herein suggest that the weight gain observed after ENG implant placement is no worse than that identified after use of other contraceptive methods or in women unexposed to exogenous sex steroids [2–4].

A 2010 review by Verhaeghe et al. focusing on hormonal contraceptive choices available for women in Europe with features of the metabolic syndrome found that the ENG implant does not

Table 1

Pairwise comparisons of anthropometric parameters, fasting blood glucose, lipid profile, and blood pressure measurements at baseline, 1, 2, and 3 years after etonogestrel implant placement in 213 healthy women. Data expressed as median and interquartile range.

| Variable | T0 (n=213) | T1 (n=74) | T2 (n=105) | T3 (n=150) | P |
|--------------------------|-------------------------|-----------------------------|-----------------------------|---------------------------|----------------------|
| Weight (kg) | 63.3 (59.9–73.0) | 63.4 (57.6–69.3) | 65.5 (58.0–74.8) | 66.1 (59.2–78.8) | 0.16 |
| BMI (kg/m ²) | 24.7 (21.9–27.6) | 24.7 (22.9–27.2) | 25.7 (22.5–29.1) | 25.7 (22.8–30.2) | 0.05 |
| FBG (mg/dL) | 85 (81–90) ^a | 92 (86.5–94.5) ^b | 89 (82–93) ^b | 88 (82.5–94) ^b | 0.002 ^a |
| TC (mg/dL) | 172 (149–194.7) | 166 (143.7–192) | 171.5 (147–195.7) | 161.5 (141.5–185.7) | 0.08 |
| HDL (mg/dL) | 53 (45–63) ^b | 44.5 (42–50.2) ^a | 49 (42.2–55.0) ^a | 46 (41–56) ^a | 0.0001 ^{**} |
| LDL (mg/dL) | 100.5 (77.2–118.7) | 106 (86–115.7) | 110 (88–129.2) | 98.5 (81–116.7) | 0.08 |
| TG (mg/dL) | 75 (55–100) | 58 (45.2–80.5) | 63 (44.2–89.7) | 69.5 (51.0–96.7) | 0.09 |
| SBP (mmHg) | 110 (110–120) | 110 (110–120) | 110 (100–120) | 110 (100–120) | 0.44 |
| DBP (mmHg) | 70 (60–80) | 70 (60–75) | 70 (60–80) | 70 (60–80) | 0.97 |

BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; DBP, diastolic blood pressure; FBG, fasting blood glucose; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides. ^{a,b} Same letters do not differ at the 5% significance level (Bonferroni test). T0, baseline (prior to implant placement); T1, 1 year post-implant; T2, 2 years post-implant; T3, 3 years post-implant.

^a T0 vs. T2 and T0 vs. T3 (ANOVA, Tukey's post-hoc test).

^{**} T0 vs. T1, T0 vs. T2 and T0 vs. T3 (ANOVA, Tukey's post-hoc test).

Download English Version:

<https://daneshyari.com/en/article/3919215>

Download Persian Version:

<https://daneshyari.com/article/3919215>

[Daneshyari.com](https://daneshyari.com)